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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,620	10/12/2001	William H. Frey II	PP16156.002 (35784/239423	1674

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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,620	FREY, WILLIAM H.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election **with** traverse of Group I (claims 1-12) drawn to a method for preventing or rescuing ischemic damage in the central nervous system of a mammal in Paper No. 6 (2 May 2003) is acknowledged. The traversal is on the ground(s) that the broad scope of Group I's preamble is encompassed in the more narrow scope of Group II. In addition the two Groups have common clinical endpoints and near identical method steps. This is found persuasive. Groups I and II are hereby rejoined.

2. Claims 1-26 are under examination.

Drawings

3. The drawings are objected to because Figures 7, 8, 9, and 10 each have three separate graphs, each of which should be appropriately labeled in both the Specification and the corrected drawings (i.e. "7A, 7B, 7C"). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims **1-26** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of *reducing* ischemic damage in the central nervous system of a mammal said method comprising administering intranasally (IN) a therapeutically effective amount of insulin-like growth factor-1 (IGF-1) or biologically active variant thereof, does not reasonably provide enablement for a method of *preventing* ischemic damage in the central nervous system of a mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

5. "Prevention" is understood in the art to mean a total protection from disease or injury (Stedman's Medical Dictionary). Thus, given the high level of required effect, a high level of evidence showing prevention is also required. While the specification demonstrates a level of protection of the central nervous system to ischemic harm, total prevention was not achieved.

6. In conclusion, due to the large quantity of experimentation necessary to achieve prevention, the lack of direction/guidance presented in the specification regarding prevention, the absence of working examples directed to examples of prevention, the complex nature of the invention, the unpredictability of the effects of biologically active variants and growth factors on cells and/or patients [Guan *et al.* (July 1993) "The Effects of IGF-I Treatment After Hypoxic-Ischemic Brain Injury in Adult Rats." Journal of Cerebral Blood Flow and Metabolism **13**(4): 609-616], and the breadth of the claims which fail to recite limitations for what constitutes prevention of ischemic damage by IGF-I, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Obviousness-Type Nonstatutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims **1-26** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-44 of copending Application No. 10/114385 [United States Patent Application Publication US 2002/0169102 A1 14 November 2002) Frey II]. This is a provisional obviousness-type double patenting rejection. Although the claims are not identical, they are not patentably distinct from each other because the claims of US 2002/0169102 A1 are directed to a method for the treatment of a central nervous system disorder in a mammal, said method comprising administering a composition comprising IGF-I to the nasal cavity of said mammal wherein the central nervous system disorder is ischemia and the effective amount of IGF-I is from about 0.002 mg/kg body weight to about 2.0 mg/kg of body weight thus meeting the limitations of claims 1-26.

8. Claims **1-26** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-34 of U.S. Patent No. 6407061 B1 (18 June 2002) Frey II. Although the claims are not identical, they are not patentably distinct from each other because the claims of US 6407061 are directed to a method for administering an insulin-like growth factor to a brain of a mammal comprising applying a pharmaceutical composition comprising an effective amount of a insulin-like growth factor to the nasal cavity of said mammal in an amount effect for promoting growth of a brain cell, promoting survival of a brain cell, augmenting activity of a brain cell, providing a protective effect on a brain cell, or a combination thereof. US 6407061 also claims said method wherein the IGF-I is administered for treating a neurological condition, a brain disorder, a psychiatric disorder, or a combination thereof including stroke thus meeting the limitations of claims 1-26.

9. Claims **1-26** are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6407061 B1 (18 June 2002) Frey II. US 6407061 teaches a method for administering an insulin-like growth factor to a brain of a mammal comprising applying a pharmaceutical composition comprising an effective amount of a insulin-like growth factor to the nasal cavity of said mammal in an amount effect for promoting growth of a brain cell, promoting survival of a brain cell, augmenting activity of a brain cell, providing a protective effect on a brain cell, or a combination thereof. US 6407061 also teaches a method wherein IGF-I is administered for treating a neurological condition, a brain disorder, a psychiatric disorder, or a combination thereof including stroke thus meeting the limitations of claims 1-26 (Claims 1-34).

10. It would have been obvious to a person of ordinary skill in the art at the time of the invention to use the method as taught by US 6407061 to use IGF-I to treat stroke because stroke often results in the loss of brain cells, both neurons and glia and the method as taught by US 6407061 is to treat such damage (Col. 1 and 2). A person of ordinary skill in the art at the time of the invention would have been motivated to use the method of US 6407061 because of the success taught by US 6407061 of using IGF-I to promote the growth of a brain cells and in promoting the survival of brain cells (Col. 1-3). A person of ordinary skill in the art at the time of the invention would have a reasonable expectation of success because US 6407061 taught the successful delivery of IGF-I via an intranasal route (Col. 1-3).

11. The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or

subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

12. Claims **1-26** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 6180603 B1 (30 January 2001) Frey II. Although the claims are not identical, they are not patentably distinct from each other because the claims of US 6180603 are directed to a method for administering an insulin-like growth factor to a brain of a mammal comprising applying a pharmaceutical composition comprising an effective amount of a insulin-like growth factor to the nasal cavity of said mammal in an amount effect for promoting growth of a brain cell, promoting survival of a brain cell, augmenting activity of a brain cell, providing a protective effect on a brain cell, or a combination thereof. US 6180603 also claims said method wherein the IGF-I is administered for treating a neurological condition, a brain disorder, a psychiatric disorder, or a combination thereof including stroke thus meeting the limitations of claims 1-26.

13. Claims **1-26** are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6180603 B1 (30 January 2001) Frey II. US 6180603 teaches a method for administering an insulin-like growth factor to a brain of a mammal comprising applying a pharmaceutical composition comprising an effective amount of a insulin-like growth factor to the nasal cavity of said mammal in an amount effect for promoting growth of a brain cell, promoting survival of a brain cell, augmenting activity of a brain cell, providing a protective effect on a brain cell, or a combination thereof (claims 1-41). US 6180603 also teaches a method wherein the IGF-I is

administered for treating a neurological condition, a brain disorder, a psychiatric disorder, or a combination thereof including stroke thus meeting the limitations of claims 1-26 (Col. 2).

14. It would have been obvious to a person of ordinary skill in the art at the time of the invention to use the method as taught by US 6180603 to use IGF-I to treat stroke because stroke is a species of the genus, neurological condition, as taught by US 6180603 (Col. Lines 44-55). A person of ordinary skill in the art at the time of the invention would have been motivated to use the method of US 6180603 because of the success taught by US 6180603 of using IGF-I to treat a neurological condition (Col. 1 lines 42-63). A person of ordinary skill in the art at the time of the invention would have a reasonable expectation of success because US 6180603 taught the successful delivery of IGF-I via an intranasal route (Col. 2 lines 20-65).

15. The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the

claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Summary

16. Claims 1-26 are hereby rejected.

17. The following articles and patents were found by the Examiner during the art search for the instant Application and are here made of note:

a. US 6313093 B1 (6 November 2001) Frey II

b. US 5624898 (29 April 1997) Frey II

c. US 2003/0072793 A1 (17 April 2003) Frey II *et al.*

d. Johnston *et al.* (January 1996) "Insulin-like Growth Factor-1 is a Potent Neuronal Rescue Agent after Hypoxic-Ischemic Injury in Fetal Lambs." J. Clin. Invest. **97**(2): 300-308.

e. US 2002/0072498 A1 (13 June 2002) Frey II

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C Kemmerer

CJN
June 20, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER